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Pitout JDD, Church DL, Gregson DB, Chow BL, McCracken M, Mulvey M, Laupland KB (2007). Molecular epidemiology of CTXM-producing *Escherichia coli* in the Calgary Health Region: emergence of CTX-M-15-producing isolates. *Antimicrob. Agents Chemother.* 51: 1281-1286.

Pelczar JR, Harley JP, Klein DA (1993). *Microbiology: Concepts and Applications.* McGraw-Hill Inc., New York, pp. 591-603.

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Full Length Research Paper

Formula for estimating incidence of chronic diseases from prevalence, mortality, and other indices from survey

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A theoretical formula was devised to calculate the age-specific estimated incidence (ASEI) rate of chronic diseases using consecutive-year data on disease prevalence and death rate. Data on the rate of persons who had suffered from one disease but died from another disease (RPDA) were retrieved from the database of a public health center. The ASEI rate of diabetes mellitus (DM) and hypertension among older age groups was found to be negative. After correcting for RPDA, the ASEIs of DM became positive or nearly 0 for this age group. It is surmised that the negative ASEIs of hypertension could be improved by considering the multiple diseases of a patient in the patient survey and finding through practicable research in the same patient survey, the rate of persons who suffered from a disease that developed into another disease (RPCA). Additional research efforts that include other factors such as the estimated cure rate (ECR) and the estimated potential incidence ratio (EPIR) were discussed. The formula for the ASEI was consequently arrived at by taking all of these elements of the RPDA, RPCA, ECR, and EPIR into consideration.

Key words: Incidence, prevalence, cure rate, rate of persons who had suffered from one disease but died from another disease (RPDA), rate of persons who suffered from a disease that developed into another disease (RPCA), survey.

INTRODUCTION

The incidence rate is usually calculated by the following formula and is not determined as a minus value (Armitage et al., 2002):

$$I = \frac{\text{number of new cases in any given period}}{\text{population at risk}}$$

The incidence rate is calculated from a follow-up research study, but in any cohort, there will be a change in the population because of migration (Preston et al., 2007). Thus, the research will be expensive and time-consuming.

The outcome of chronic diseases between year a and the consecutive year b is shown in Figure 1. Square A represents the number of patients in year a , and square B the number in year b . If a cure is not considered, the incidence of a chronic disease can be calculated using the data of patients in consecutive years a and b and the data of deaths between years a and b using the following formula:

$$I = B - A + D$$

According to the method for estimating incidence from

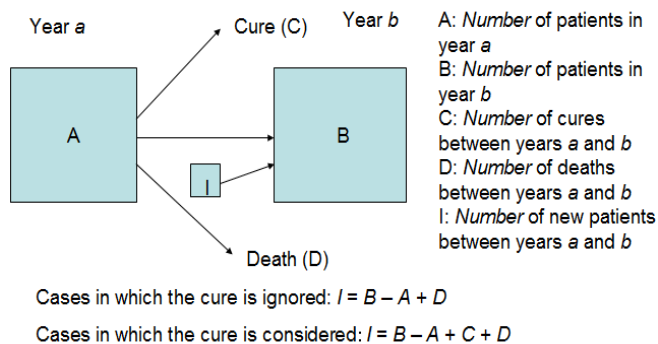


Figure 1. Outcome on chronic diseases between year *a* and consecutive year *b*.

prevalence and mortality, Leske et al. (1981), Dewey (1992), and Hill et al. (1999) reported that glaucoma, dementia, and diabetes are irreversible diseases. They were not considered for the cure rate or other necessary indices. So, the methods by them could not be used for common chronic diseases. The author studied the possibility of calculating the incidence rate using statistical data through the following steps and arrived at

It is assumed that the consecutive years are *a* and *b*.

The following are the values used for calculation in this study :
 range of all age groups as *w* is 5 and, accordingly, $w = b - a = 5$.

Thus, the midyear between years *a* and *b* is calculated as $\frac{a + b}{2}$.

The *i*th age group is the group aged between $w \times i$ years and $w \times (i + 1) - 1$ years ($i = 0, 1, 2, \dots, 16$).

The cohort of the population in the *i*th age group in year *a* is ${}_aG_i$, the population is ${}_aN_i$, the prevalence is ${}_aP_i$, the death rate of a particular disease for ${}_aG_i$ between years *a* and *b* is ${}_ad_i$, and the rate of all deaths for ${}_aG_i$ is ${}_aD_i$.

Similarly, for year *b*,

the number of patients in year *a* for ${}_aG_i$ is ${}_aP_i \times {}_aN_i$, that in year *b* for ${}_aG_i$ is ${}_bP_{i+1} \times {}_bN_{i+1}$, and the number of deaths for ${}_aG_i$ between years *a* and *b* is ${}_ad_i \times {}_aN_i$.

Thus, the increase in the number of patients for ${}_aG_i$ between years *a* and *b*

is ${}_bP_{i+1} \times {}_bN_{i+1} - {}_aP_i \times {}_aN_i + {}_ad_i \times {}_aN_i$.

Therefore, the estimated incidence rate for ${}_aG_i$ is $\frac{{}_bP_{i+1} \times {}_bN_{i+1} - {}_aP_i \times {}_aN_i + {}_ad_i \times {}_aN_i}{{}_aN_i}$

$$= \frac{{}_bP_{i+1} \times {}_bN_{i+1} - {}_aP_i + {}_ad_i}{{}_aN_i}$$

Thus, the estimated incidence rate per year at the midyear between years *a* and *b*

$$\text{is } \frac{{}_bP_{i+1} \times {}_bN_{i+1} - {}_aP_i + {}_ad_i}{{}_aN_i} \times \frac{1}{b - a} \dots \text{Formula 1.}$$

The denominator of this formula includes ${}_aN_i$ and not $\frac{{}_a+bN_i}{2}$, because the concept of the cohort of ${}_aG_i$ is used. The value calculated

using formula 1 for the 0 to 4-year age group in 2000 and the 5 to 9-year age group in 2005 reflects the estimated incidence rate for the 2.5 to 7.5-year age group at the midyear of the period 2000 to 2005. The midpoints of the age groups for the estimated incidence rates are 5, 10, 15, 20, etc., up to the age of 80 years.

Formula 1.

1. A theoretical formula was derived for the incidence rate in different age groups by ignoring the cure rate.
2. The rate of change in the population of Japan by migration was researched, and its influence on the formula is discussed.
3. The prevalence in the patient survey was compared

with that in other researches, and whether the data were appropriate for the calculation of the ASEI was discussed. 4. Using the data obtained from patient surveys and death rates, the theoretical formula for the estimated incidence rate was tested and discussed for the necessary data. The formula for estimating the incidence rate was arrived at by taking into consideration the necessary data.

MATERIALS AND METHODS

A theoretical formula for calculating the age-specific estimated incidence rate by disregarding the cure rate and using statistical data for consecutive years. The following theoretical formula was derived by disregarding the cure rate.

Thus, the j th age group is the group aged between $w \times j + w/2$ years and $w \times (j + 1) + w/2$ years ($j = 0, 1, 2, \dots, 15$).

Formula 1 can then be rewritten as follows:

$$\text{When } {}_bN_{i+1} = (1 - {}_aD_i) \times {}_aN_i, \quad \frac{{}_a+bR_j}{2} = \frac{{}_bP_{i+1} \times (1 - {}_aD_i) - {}_aP_i + {}_ad_i}{b - a} \dots \text{Formula 2.}$$

The prevalence used in formula 1 or 2 was estimated using data from the patient survey with stratified random sampling of all residents of Japan, including foreigners (Jerrold, 1999; Rothman and Greenland, 1998; Statistics and Information Department Minister's Secretariat Ministry of Health, Labour and Welfare Japanese Government, 2009). Thus, the value calculated using formula 1 or 2 is referred to as the age-specific estimated incidence rate (ASEI). Formula 1 or 2 was used for the cohort; however, if the composition of the population in the group expressed as ${}_aG_i$ changed owing to migration, this formula may not be applicable. Therefore, the rate of change in the population owing to the migration of ${}_aG_i$ between 2000 and 2005 was investigated.

From the calculation, using both the data on foreigners residing in Japan and those on Japanese nationals who went overseas over a period of 3 months in each age group between 2000 and 2005, the maximum rate was estimated to be 4.6% of the population for the age group 20 to 24 years. The rate of change in the population is considerable in some instances; however, this possibility was not considered for the cohort of this study in formula 1 or 2. However, the rate of change was considered the same for all the areas of random sampling in the patient survey; thus, no correction was needed (Jerrold, 1999; Rothman and Greenland, 1998).

Estimated prevalence from patient surveys

The Ministry of Health, Labour, and Welfare of Japan conducted

$$\text{No. of patients} = \frac{\text{No. of patients in one disease (one attribution) in research sample} \times \text{Total no. of patients in all institutions in the static research}}{\text{Total no. of patients in sample institutions in the patient survey in static research}} \quad (\text{Formula 3})$$

For patients with more than one disease, a single disease was selected for consideration. The patients were classified by the Ministry of Health, Labour, and Welfare of Japan according to the International Classification of Diseases (ICD); specifically, the same

patient surveys in Japan in October 1999, 2002, and 2005. The research was done according to the stratification of medical institutions, such as the 11 types of hospitals classified by the property or the number of beds, clinics, and dental clinics in the secondary medical service areas (secondary emergency medical areas) of the prefectures. The primary emergency medical areas are clinics, the secondary emergency medical areas are hospitals, and the third emergency medical areas are hospitals with a high level of service (Ministry of Health, Labour and Welfare, 2006).

Static research was conducted on medical institutions according to the number of patients and the property or number of beds, and the resulting data were used to estimate the number of patients in the patient survey. In the static research on medical institutions, the total number of outpatients in September and the total number of inpatients on the 30th day in September were researched and used for the formula in the patient survey (Statistics and Information Department Minister's Secretariat Ministry of Health, Labour and Welfare Japanese Government, 2009). For patients in hospitals or clinics, data were recorded for one day in the patient survey. Practical formulae are shown in Table 1. The standard error of the number of patients is calculated using the approximate expression for the ratio of the two variances (Armitage et al., 2002; Statistics and Information Department Minister's Secretariat, Ministry of Health, Labour and Welfare Japanese Government. 2000). These formulae indicate that

ICD classification was used for issuing death certificates (World Health Organization, 2004). The consultation rate for medical care was calculated as:

$$\text{Consultation rate for medical care} = \frac{\text{No. of inpatients} + \text{No. of outpatients}}{\text{Population}}$$

The estimated number of patients, including those who did not receive medical care on the research day, was calculated using the following formula developed by several investigators (Statistics and

Information Department Minister's Secretariat Ministry of Health, Labour and Welfare Japanese Government, 2009; Sota, 1960; Hashimoto et al., 1994; Nakamura et al., 1994)

$$\text{Estimated number of patients} = \text{Inpatients} + \text{Outpatients (first visit)} + \text{Outpatients (following visit)} \times \text{Average interval since last visit} \times \text{adjustment factor (6/7)} \quad (\text{Formula 4}).$$

Hashimoto et al. (1994) suggested that patients revisiting the clinic after an interval of over 31 days should be considered first-time

Table 1. Formula for the calculation of the number of patients in hospitals and clinics in patient survey of Japan.

Variable	Formula	Comment
Hospital	$Z_{gkh} = \sum_{j=1}^7 \left[\frac{X_{gjk}}{X'_{gjk}} \times \frac{W_{gikh}}{Y'_{gj}} \times Y_{gj} \right] + \frac{\sum_{j=8}^{11} \frac{N_{gj}}{n_{gj}} X_{gjk}}{\sum_{j=8}^{11} \frac{N_{gj}}{n_{gj}} X'_{gjk}} \times \frac{\sum_{j=8}^{11} \frac{N_{gj}}{n_{gj}} W_{gikh}}{\sum_{j=8}^{11} \frac{N_{gj}}{n_{gj}} Y'_{gj}} \times \sum_{j=8}^{11} Y_{gj}$ <p>Z_{gkh}: Estimated number of patients by some disease (attribution) (h) by sex (k) and by secondary emergency medical areas (g). N_{gj}: Number of medical institutions by stratified class (j) in secondary emergency medical areas (g) in the static research on medical institutions. n_{gj}: Number of medical institutions by stratified class (j) in secondary emergency medical areas (g) in the patient survey. X_{gjk}: Number of patients by sex (k) in stratified class (j) in secondary emergency medical areas (g) in the patient survey. X'_{gjk}: Number of patients by odd-numbered birthday by sex (k) in stratified class (j) in secondary emergency medical area (g) in the patient survey. W_{gikh}: Number of patients by odd-numbered birthday by some attribution (h) by sex (k) by stratified class (j) in secondary emergency medical areas (g) in the patient survey. Y'_{gj}: Number of patients in the sample institutions (in the patient survey) by stratified class (j) in secondary emergency medical areas (g) in the static research (beds and department) on medical institutions. Y_{gj}: Number of patients by stratified class (j) in secondary emergency medical areas (g) in the static research on medical institutions.</p>	<p>W_{gikh}: the index to be inputted by the research of patient survey.</p> <p>The attribution refers to the ICD classification of the disease. 1: Psychiatry hospitals 2: Infectious disease medical hospitals 3: Tuberculosis medical hospitals 4: High-level medical hospitals 5: Senile dementia medical hospitals 6: Hospitals providing bedridden care for senile persons 7: Hospitals providing beds for senile diseases 8: (except upper 1-7 cases) Number of beds is under 99. 9: (except upper 1-7 cases) Number of beds is between 100 and 299. 10: (except upper 1-7 cases) Number of beds is between 300 and 499. 11: (except upper 1-7 cases) Number of beds is more than 500.</p>
Clinic	$Z_i = \frac{\sum_{j=1}^L X_{ij}}{\sum_{j=1}^L Y'_{ij}} \times Y_i = \frac{\sum_{s=1}^{Ni} X_{i(s)}}{\sum_{s=1}^{ni} Y'_{i(s)}} \times Y_i$ <p>Z_i: Estimated number of patients by some attribution in a prefecture area (i). L: Number of stratified classes in the prefecture. X_{ij}: Number of patients by some attribution in a stratified class (j) in a prefecture area (i) in the patient survey. Y'_{ij}: Number of patients in the sample institutions (in the patient survey) by stratified class (j) in a prefecture area (i) in the static research on medical institutions. Y_i: Number of patients by prefecture area (i) in the static research on medical institutions. $X_{i(s)}$: Number of patients by some attribution in some institutions (s) in a prefecture area (i) in the patient survey. $Y'_{i(s)}$: Number of patients in sample institutions (s) (in the patient survey) in prefecture area (i) in the static research on the medical institutions. ni: Number of sample institutions (in the patient survey) in a prefecture area (i).</p>	<p>X_{ij} or $X_{i(s)}$: the index to be inputted by the research of patient survey.</p>

visitors and the survey have been conducted according to their suggestion (Statistics and Information Department Minister's Secretariat, Ministry of Health, Labour and Welfare Japanese Government. 2000; Hashimoto et al., 1994). The average interval since last visit was calculated for every prefecture, age group, sexual group, and ICD classification in the surveys. The inpatients and outpatients were calculated separately and then added. The total number of patients was calculated by summarizing the number of patients in every prefecture. The estimated prevalence (hereafter referred to as "prevalence") for different age groups was calculated by dividing the estimated number of patients by the total population of Japan as the point prevalence (Rothman and Greenland, 1998). The prevalence in 2005 was used from the data of 2005. The prevalence in 2000 was interpolated from the data of 1999 and 2002.

1999 and 2002. The prevalence in the 5 to 9-year age group in 2000 positively correlated with that of the 4 to 8-year age group in 1999 and the 7 to 11-year age group in 2002. In the different age groups in 2000, the prevalence was calculated as follows:

- 4 to 8-year age group in 1999: $(1/5 \times \text{prevalence in the 0 to 4-year age group}) + (4/5 \times \text{prevalence in the 5 to 9-year age group})$.
- 7 to 11-year age group in 2002: $(3/5 \times \text{the 5 to 9-year age group}) + (2/5 \times \text{the 10 to 14-year age group})$.
- 5 to 9-year age group in 2000: $(2/3 \times \text{the 4 to 8-year age group in 1999}) + (1/3 \times \text{the 7 to 11-year age group in 2002})$.
- > 9-year age group in 2000: similarly calculated.
- 0 to 4-year age group in 2000: $(2/3 \times \text{the 0 to 3-year age group in 1999}) + (1/3 \times \text{the 2 to 6-year age group in 2002})$.

The standard errors for the age groups in 2000 were calculated using the same method.

Calculation of death rate from statistical data

The death rate between 2000 and 2005 is calculated as follows:

${}_a d_i$ is the death rate between 2000 and 2005, which corresponds to the death rate between years a and b in formula 1 or 2,

$${}_{2000} d_i + {}_{2001} d_i \times 4/5 + {}_{2001} d_{i+1} \times 1/5 + {}_{2002} d_i \times 3/5 + {}_{2002} d_{i+1} \times 2/5 + {}_{2003} d_i \times 2/5 + {}_{2003} d_i \times 3/5 + {}_{2004} d_i \times 1/5 + {}_{2004} d_{i+1} \times 4/5,$$

because each age group becomes 1 year older after a year. The ${}_a D_i$ between 2000 and 2005 is calculated in the same manner. By the above formula, ${}_{2005} N_{i+1}$ corresponds considerably to $(1 - {}_a D_i) \times {}_{2000} N_i$ [18].

Test 1 for the ASEI

The categories of the International Classification of Diseases (10th

Revision; ICD-10) used this to test the validity of the formula included for diabetes mellitus (DM, E10-14), hypertensive diseases (I10-15), and cerebrovascular diseases (I60-69).

From formula 2, when it is assumed that $(1 - {}_a D_i)$ and ${}_a d_i$ are constant values, ${}_b P_{i+1}$ and ${}_a P_i$ are two independent random variables [19].

Thus, the standard error (SE) of $\frac{{}_{a+b} R_j}{2}$ is

$$SE(\frac{{}_{a+b} R_j}{2}) = \frac{1}{b-a} \sqrt{\{SE({}_b P_{i+1}) \times (1 - {}_a D_i)\}^2 + \{SE({}_a P_i)\}^2} \dots \text{Formula 5.}$$

The ASEI (SE) were calculated from formulae 2 and 5 using the prevalence in 2000 and 2005, and death rate between 2000 and 2005.

Formula 2 for the ASEI and test 2

If one follows the hypothesis that the death rate of persons suffering from a certain disease, say S , does not include the rate of persons who had been suffering from disease S but may have died from another disease, then the ASEI of disease S calculated using formula 1 or 2 could be incorrect because the death rates used were incorrectly. Hence, the number of such persons was obtained from the database of death certificates of a public health center which covered the period 1992 to 1998. However, this area differs from that in the sample in the patient surveys. The value is referred to as the rate of persons who died from another disease (RPDA). The number of all deaths between 1992 and 1998 is 4126, with a mean number per year of 589. The figure included cases of DM and other chronic diseases when disease S was not recorded as the cause of death but was recorded as the other continuous disease until the time of death. The rates and standard errors were calculated as follows (Miller, 1983b):

$$RPDA = \frac{\text{number of persons who died from another disease}}{\text{number of all deaths}}$$

$$(SE) RPDA = \sqrt{\frac{RPDA(1 - RPDA)}{\text{number of all deaths}}}$$

The resultant RPDA values and SE for different age groups are shown in Table 2. The death rate corrected by considering the RPDA was calculated as follows: death rate 2 = death rate + rate of all deaths \times RPDA and death rate 3 = death rate + rate of all deaths \times {RPDA + 1.96 \times SE (RPDA)}. ASEI2 was calculated from death rate 2 and ASEI3 from death rate 3. The hypothesis that ASEI = ASEI2 was tested as follows (Miller, 1983c):

$$z0 = \frac{(ASEI2 - ASEI)}{SE(ASEI)}$$

As this sample (a public health center) did not correspond to the sample of patient surveys in Japan, this test was considered a pilot test for the above hypothesis.

Validity of prevalence in patient survey

To test the validity of the prevalence in the patient survey, data from the National Health and Nutrition Survey in 2006 was used for comparison. In this research, the data included the rate of persons within age groups who failed drug therapy for hypertension or DM (Office for Life-Style Related Diseases Control in Ministry of Health, Labour and Welfare of Japan, 2007). The 2006 survey was conducted with a stratified random sample of 5,000 family units from Japan; the sampling rate was 0.005% of the population, and the significance of the proportion was tested (Miller, 1983d).

Table 2. Rates^a and standard errors of the rate (per 1000 population) of person aged over 50 years who have died due to another disease (RPDA) according to chronic diseases among the ICD-10 categories obtained from the database of a public health center^b in Japan between the years 1992 -1998.

Classification of disease	Rate (S.E)									
	Total	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-above
E10-14 Diabetes mellitus	12.6 (1.7)	0.0 (0.0)	8.1(8.0)	14.0 (8.0)	17.6 (7.1)	15.2 (6.2)	26.4 (7.0)	10.2 (3.6)	8.1 (3.3)	5.8 (2.9)
F00-09 Organic including symptomatic mental disorders	3.6 (0.9)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	2.9 (2.9)	0.0 (0.0)	3.8 (2.7)	6.3 (2.8)	5.4 (2.7)	4.4 (2.5)
G20 Parkinson's disease	2.2 (0.7)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	2.9 (2.9)	7.6 (4.4)	5.6 (3.3)	2.5 (1.8)	0.0 (0.0)	0.0 (0.0)
I00-99 Diseases of the circulatory system	38.8 (3.0)	12.2 (12.1)	24.2 (13.8)	9.3 (6.6)	32.4 (9.6)	50.6 (11.0)	41.4 (8.6)	31.7 (6.2)	63.3 (8.9)	42.2 (7.7)
I10-15 Hypertensive diseases	10.2 (1.6)	0.0 (0.0)	8.1 (8.0)	9.3 (6.6)	2.9 (2.9)	12.7 (4.0)	7.5 (3.8)	12.7 (4.0)	14.8 (4.4)	8.7 (3.5)
I20-25 Ischemic heart disease	5.1 (1.1)	0.0 (0.0)	0.0 (0.0)	4.7 (4.7)	5.9 (4.1)	2.5 (2.5)	1.9 (1.9)	5.1 (2.5)	8.1 (3.3)	8.7 (3.5)
I45-49 Cardiac dysrhythmias	2.7 (0.8)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	2.9 (2.9)	2.5 (2.5)	3.8 (2.7)	3.8 (2.2)	4.0 (2.3)	1.5 (1.5)
I60-69 Cerebrovascular diseases	41.7 (3.1)	12.2 (12.1)	40.3 (17.7)	9.3 (6.6)	26.5 (8.7)	55.7 (11.5)	52.7 (9.7)	36.8 (6.7)	59.3 (8.7)	46.6 (8.0)
I70 Atherosclerosis	5.6 (1.2)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	3.8 (2.7)	10.2 (3.6)	8.1 (3.3)	10.2 (3.8)
J40-47 Chronic lower respiratory disease	8.0 (1.4)	0.0 (0.0)	8.1 (8.0)	4.7 (4.7)	5.9 (4.1)	5.1 (3.6)	16.9 (5.6)	8.9 (3.3)	8.1 (3.3)	7.3 (3.2)
J43 Emphysema	1.5 (0.6)	0.0 (0.0)	0.0 (0.0)	4.7 (4.7)	2.9 (2.9)	5.1 (3.6)	0.0 (0.0)	1.3 (1.3)	1.3 (1.3)	0.0 (0.0)
J45 Asthma	3.9 (1.0)	0.0 (0.0)	8.1 (8.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	9.4 (4.2)	5.1 (2.5)	4.0 (2.3)	4.4 (2.5)

RESULTS

The prevalence in 2000 and 2005 for different age groups, the ASE1 (SE), ASE2, and ASEI3 for DM, hypertensive diseases, and cerebrovascular diseases are shown in Figures 2, 3, and 4, respectively. The prevalence of DM peaked for the 70 to 74-year age group in both 2000 and 2005. The ASE1 peaked at age 60 but was negative for those > 70 years; however, ASEI2 and ASEI3 for those > 70 years were positive or closer to 0 than the ASE1. ASEI2 differed from the ASE1 in the 80-year age group, with a significance level of $p < 0.01$.

On the prevalence of hypertensive diseases, peaks were noted in the 75 to 79- and 80 to 84-year age groups in 2000 and 2005. The ASE1 peaked at 65 years but was negative at > 80

years. There was no significant difference between ASEI2 and ASEI3. No peaks were observed for the prevalence and the ASE1 of cerebrovascular diseases in both 2000 and 2005. ASEI2 was significantly higher than the ASE1 with increasing age. ASEI2 differed from the ASE1 in the 60-year age group at $p < 0.01$ and ASEI2 for >70 years differed from the ASE1 at $p < 0.001$. Many patients with cerebrovascular diseases in old age groups died by another cause, for example, aspiration pneumonia; thus, the result that the ASE1 and ASEI2 were different in old age groups is reasonable (Bruce and Steven, 1996).

The comparison of prevalence of diabetes mellitus and hypertension between the National Health and Nutrition Survey in 2006 and the patient survey in 2005 is shown in Table 3 and Figure 5. Regarding DM, there was no difference

between the two researches except for persons within 65 to 69-years old, over 70-years old, and the total. The prevalence for hypertension in the 2006 nutrition survey was significantly higher with increasing age than the prevalence for persons over 50-years old in the 2005 patient survey.

DISCUSSION

Importance of RPDA

The ASE1 of DM for >70 years is negative, and ASEI2 and ASEI3 for >70 years are positive or closer to 0 than the ASE1. These results indicate that RPDA is important in calculating the ASE1 for certain diseases, such as DM, in the older age groups. Data on RPDA of disease *S* in year *b* are acquired theoretically from retrospective research

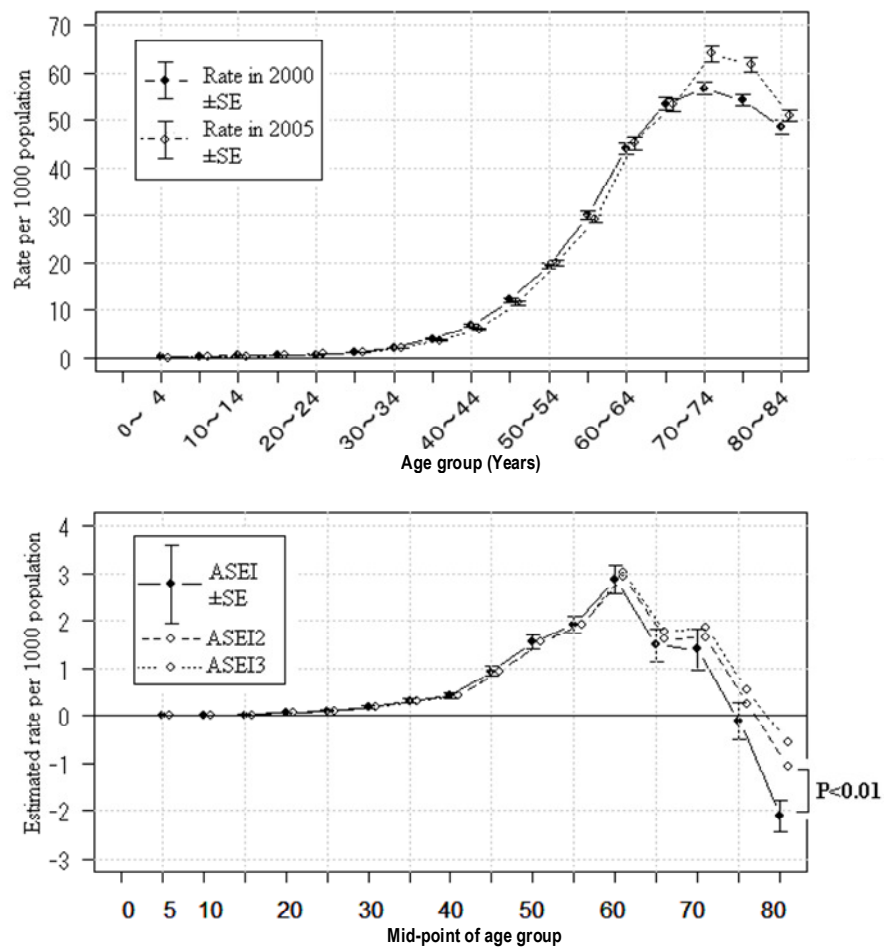


Figure 2. (a) Prevalence and (b) age-specific estimated incidence rate (ASEI) of diabetes mellitus (DM) from the data of Japan in 2000 and 2005.

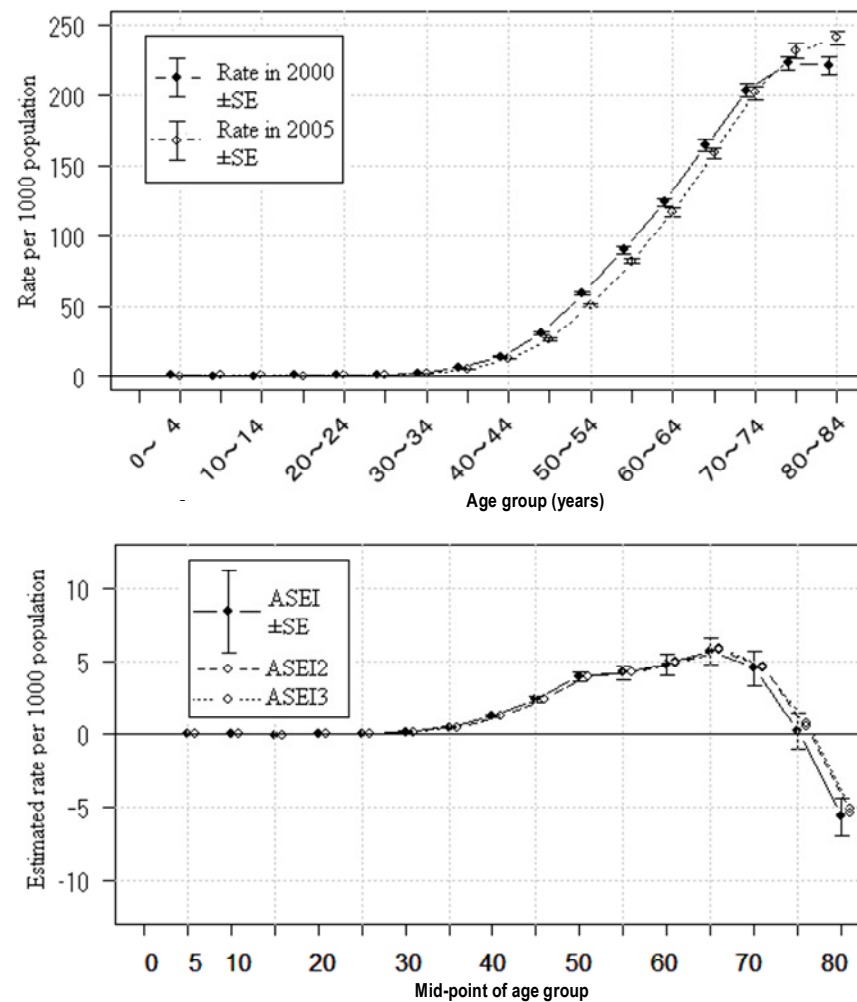


Figure 3. (a) Prevalence and (b) age-specific estimated incidence rate (ASEI) of hypertension from the data of Japan in 2000 and 2005.

Table 3. Comparison of prevalence of diabetes mellitus and hypertension within age groups between the 2006 nutrition survey and the 2005 patient survey.

Research	Age group	Total	20-29	30-39	40-49	50-59	60-69	70
National health and nutrition survey in 2006	Person of failed drug therapy for DM	204	0	2	4	29	64	105
	Rate (per 1000 population)	47.5	0.0	3.3	7.0	33.1	70.2	99.8
	Number of person received research	4296	280	607	570	875	912	1052
Patient survey in 2005	Number of DM (per 100 population)	2469	15	50	136	475	783	1013
	Prevalence (per 100 population)	23.9	1.0	2.7	8.6	24.9	49.0	55.5
	Total population of Japan	103196039	15630647	18490638	15806457	19051663	15977239	18239395
Significance between researches in 2006 and 2005		***	-	-	-	-	**	***
National health and nutrition survey in 2006	Person of failed drug therapy for hypertension	1022	2	7	22	154	300	537
	Rate (per 1000 population)	225.2	6.6	11.1	37.1	169.8	308.6	473.1
	Number of person received research	4538	301	630	593	907	972	1135
Patient survey in 2005	Number of hypertension (per 1000 population)	7809	5	55	300	1290	2189	4011
	Prevalence (per 1000 population)	75.7	0.3	3.0	19.0	67.7	137.0	219.9
	Total population of Japan	103196039	15630647	18490638	15806457	19051663	15977239	18239395
Significance between researches in 2006 and 2005		***	***	***	**	***	***	***

on the death certifications of a person of ${}_aD_i \times {}_a N_i$ and are referred as ${}_a RPDA_i$. However, research on persons of ${}_aD_i \times {}_a N_i$ is difficult owing to the large sample size. Thus, a few medical service areas in Japan should be selected, and the diseases to be studied should be narrowed down based on these model areas. Thus for a specific model area:

The ${}_a RPDA_i$ is estimated to be the $RPDA$ of the model area.

$$SE({}_a RPDA_i) = \sqrt{\frac{RPDA(1 - RPDA)}{\text{number of all deaths in the model area}}}$$

The number of deaths from disease S to be added =

$$\frac{\text{number of persons who died from another disease}}{\text{number of all deaths}} \times \frac{\text{number of all deaths}}{\text{population}} \times {}_a N_i$$

$$= {}_a RPDA_i \times {}_a D_i \times {}_a N_i \dots \text{Formula 6.}$$

Multiple diseases for one patient

In the National Health and Nutrition survey in 2006, the data concluded that the persons who did not fail due to hypertension or DM as a main disease were treated with drugs. Indeed, diseases in one patient increase or change with increasing age, especially patients who failed in hypertension could fail in cerebrovascular diseases frequently (Wade and Joey, 1996). Because of these differences in the contents between two researches, the rates of prevalence of hypertension could be different. In the old-age groups, it is common for one patient to have multiple diseases. Thus, it could be considered that the negative ASEIs in the old-age groups could be improved by considering the multiple diseases of a patient in the patient survey. The calculation could

be complicated. Thus, the multiple diseases should be narrowed down to calculate the ASEI. In Formula 4, multiple diseases of outpatients (following visit) should be counted only if these diseases are consulted on the research day. Thus, multiple diseases could reflect each other on average interval of Formula 4. The patient survey in 2008 was already conducted for the count of multiple diseases according to the life-style diseases in Japan (Statistics and Information Department Minister's Secretariat, Ministry of Health, Labour and Welfare Japanese Government, 2008).

RPCA

It is conceivable that the rate of the persons who

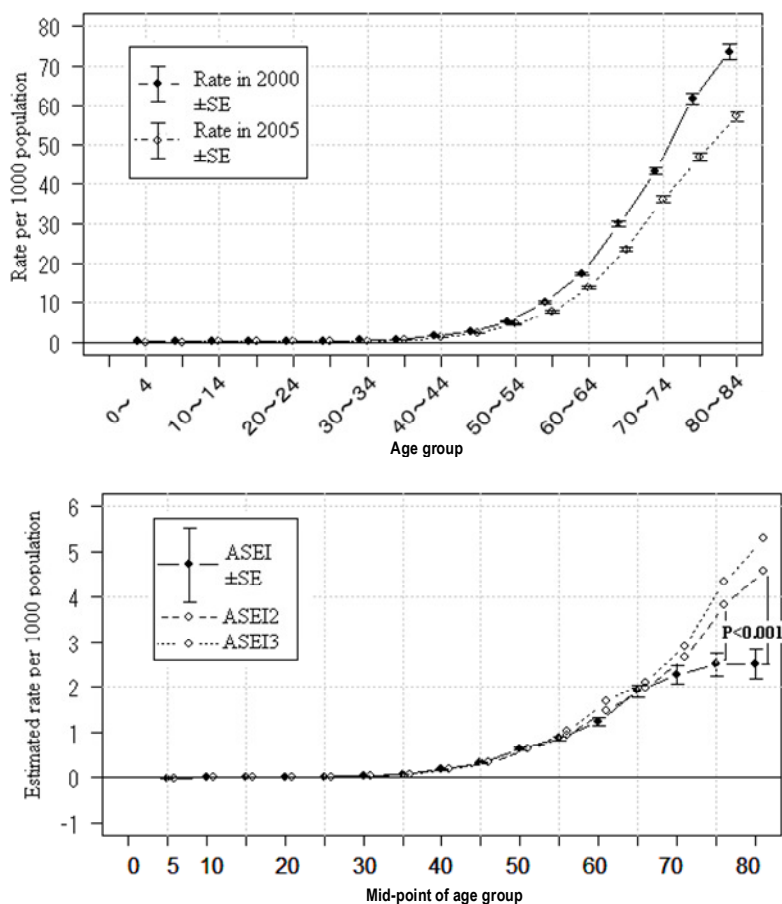


Figure 4. (a) Prevalence and (b) age-specific estimated incidence rate (ASEI) of cerebrovascular diseases from the data of Japan in 2000 and 2005.

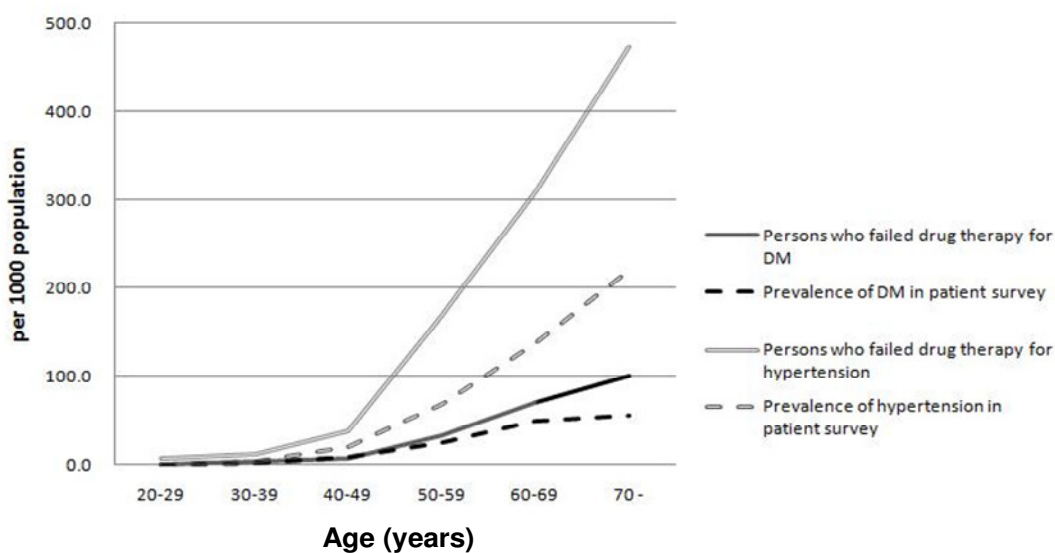


Figure 5. Comparison of prevalence of diabetes mellitus and hypertension within age groups between the 2006 nutrition survey and the 2005 patient survey.

suffered from disease *S* on the day of the patient survey in year *a* could have suffered from another disease on the day of the patient survey in year *b*. Thus, the value is referred to as the rate of persons whose disease changed to another disease (RPCA), which corresponds to RPDA. These cases were counted as new patients as they suffered from another disease and should be counted as the disease *S* in year *b* in the calculation of

$$RPCA = \frac{\sum_{i=1}^n \left[\begin{array}{l} \text{number of persons who suffered from disease } S \text{ between years } a \text{ and } b, \\ \text{and whose disease changed into another disease } (C_i) \text{ in year } b \end{array} \right]}{\sum_{i=1}^n \left[\text{number of disease } (C_i) \text{ in year } b \right]}$$

$$= \frac{\text{number of persons whose disease changed into another disease in year } b}{\text{number of all diseases in year } b}$$

When ${}_bT_i = \frac{\text{number of all diseases (as multiple diseases in one patient) in year } b}{\text{population}}$,

${}_bT_i$ is the ratio of all diseases. RPCA was acquired from retrospective research on persons of ${}_bT_i \times {}_bN_i$ in year *b*, and is referred to as ${}_bRPCA_i$.

The calculation of RPCA is complicated because the number of persons of ${}_bT_i \times {}_bN_i$ is large. Thus, few

ASEI, because the number of disease *S* patients decreased in year *b* in this case. For example, chronic hepatitis can develop into liver cirrhosis or hepatoma (Brian 1996). In Figure 6, all cases of chronic diseases between years *a* and *b* are shown. As indicated in case 4, RPCA also includes those who fail between years *a* and *b* and suffer from another disease *C* ($C_1 \sim C_n$).

medical service areas in the Japanese model were selected and disease *S* should be narrowed down for the determination of RPCA.

The total number of patients to be added

$$= \frac{\text{number of persons who suffered from the another disease in year } b}{\text{number of all diseases in year } b}$$

$$\times \frac{\text{number of all diseases in year } b}{\text{population}} \times {}_bN_i$$

$$= {}_bRPCA_i \times {}_bT_i \times {}_bN_i \cdots \text{Formula 7.}$$

According to $\frac{a+b}{2} R_j$, the number of patients to be added becomes ${}_bRPCA_{i+1} \times {}_bT_{i+1} \times {}_bN_{i+1}$ for the next age group.

Cure rate, potential incidence rate, and the formula taking into consideration the necessary factors

Patients who were found to have disease *S* during the year *a* survey should be followed up to ascertain whether they had been cured of the disease by the time the survey was conducted in year *b*. This case corresponds

to case 2 or 3 in Figure 6. The number of persons with disease *S* in year *a* is referred to as the estimated cure rate (ECR). It is not important whether patients who were cured of disease *S* suffered from another disease in year *b* or not because the other disease may not be connected with disease *S*. The ECR of disease *S* is calculated as follows:

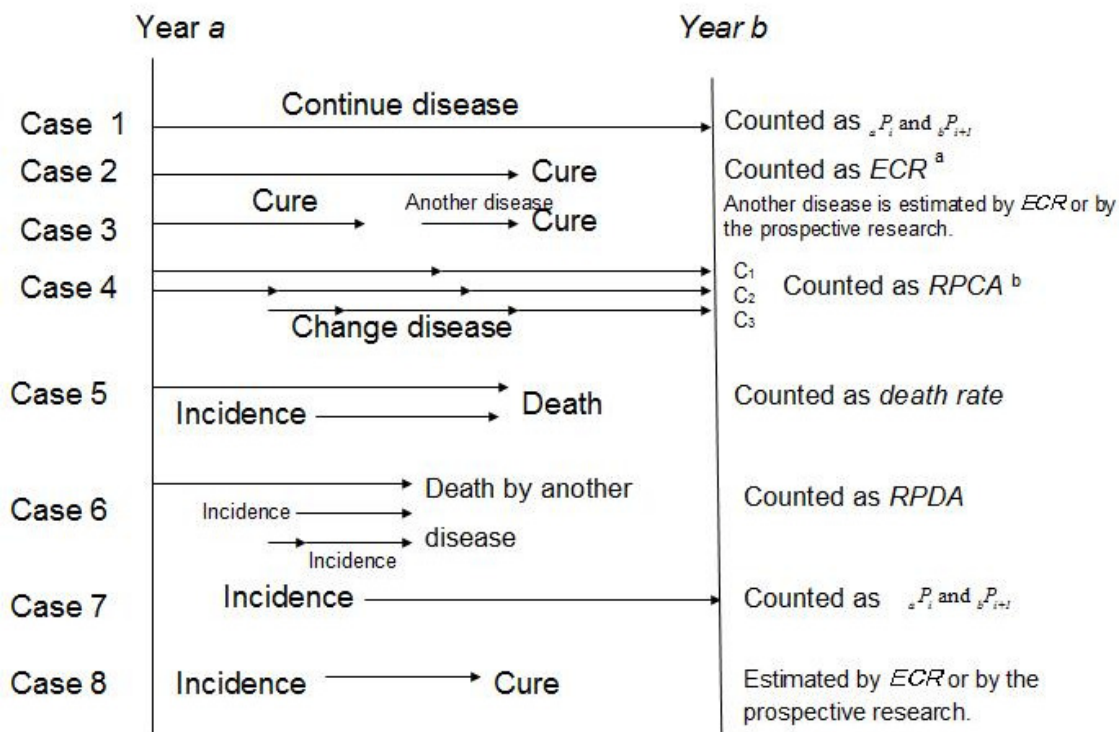


Figure 6. All cases of chronic diseases between years a and b

$$ECR = \frac{\text{number of persons who were cured of disease } S \text{ by the time year } b \text{ survey was done}}{\text{number of patients with disease } S \text{ in year } a}$$

Data of *ECR* of disease *S* was acquired on the day of the survey in year *b* based on retrospective research on persons of ${}_aP_i \times {}_a N_i$ in year *a*, referred to as ${}_a ECR_i$.

This calculation should be used in the model area like that of the *RPCA*.

The number of patients with disease *S* to be added with ${}_a ECR_i$

$$= \frac{\text{number of persons who were cured of disease } S \text{ in year } a}{\text{number of patients with disease } S \text{ in year } a} \times \frac{\text{number of patients with disease } S}{\text{population}} \times {}_a N_i$$

$$= {}_a ECR_i \times {}_a P_i \times {}_a N_i \cdots \text{Formula 8.}$$

Furthermore, there may be patients who failed to be diagnosed with the disease and were cured between years *a* and *b*. This case corresponds to case 3 or 8 in Figure 6, and the method for determining these patients could be considered using the research on the cure. According to the cured person, the number of persons there could be with no redundancy until 5 years should

be considered, and there could be 4 persons in case 1, for example, as shown in Figure 7. These numbers are added to obtain the estimated potential incidence number (EPIN). For this calculation, the disease counted in the patient survey should be recorded from the time when this disease began. However, if this method is not appropriate, it might be because prospective research for

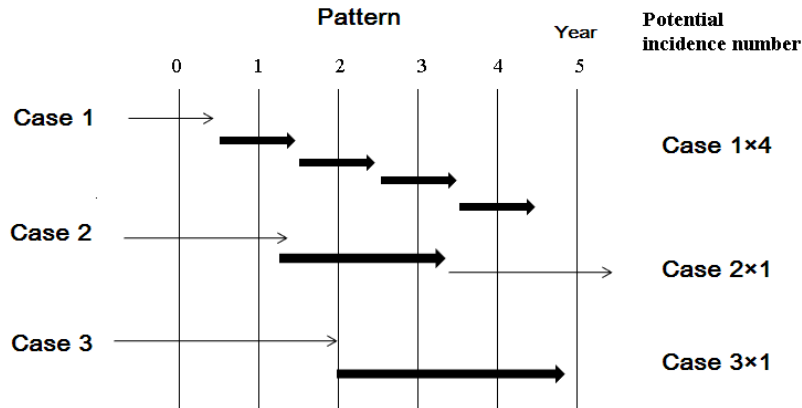


Figure 7. Estimation of potential incidence number by cure period of patients.

When the estimated potential incidence ratio (EPIR) = $EIPN / \text{the number of } {}_aP_i \times {}_aN_i$, referred to as ${}_aEPIR_i$,

$${}_aEPIR_i = \frac{{}_aEPIN_i}{{}_aP_i \times {}_aN_i}.$$

The total number of patients to be added = ${}_aEPIN_i = {}_aEPIR_i \times {}_aP_i \times {}_aN_i \dots$ Formula 9.

From Formulae 2, 6, 7, 8, and 9, the $ASEI = \frac{a+b}{2} R_j =$

$$= \frac{({}_bP_{i+1} + {}_bRPCA_{i+1} \times {}_bT_{i+1}) \times (1 - {}_aD_i) - {}_aP_i \times (1 - {}_aECR_i - {}_aEPIR_i)}{b - a}$$

$$+ \frac{{}_ad_i + {}_aRPDA_i \times {}_aD_i}{b - a}.$$

If ${}_aD_i$, ${}_bRPCA_{i+1}$, ${}_aECR_i$, ${}_aEPIR_i$, and ${}_ad_i$ are considered constant values,

$$V(ASEI) = \frac{1}{(b - a)^2} \times \left\{ (1 - {}_aD_i)^2 V({}_bP_{i+1}) + {}_bRPCA_{i+1}^2 (1 - {}_aD_i)^2 V({}_bT_{i+1}) + (1 - {}_aECR_i - {}_aEPIR_i)^2 V({}_aP_i) + {}_aD_i^2 V({}_aRPDA_i) \right\}$$

EPIN needs to be conducted.

Furthermore, patient surveys should be conducted at an interval of 5 years because the interpolation of the prevalence is not desirable, and the cohort of 5 years of age in year b or a should be surveyed retrospectively to determine RPCA, ECR, and EPIR. If recurrences occur

between years a and b , these are counted as new patients. Therefore, if these patients need to be counted, these patients should be calculated separately and the above formula could be used for people in other regions where the migration between years a and b is considerably small. In summary, the desirable design of the patient

Table 4. Desirable design of patient survey for calculation of ASEI.

Item	Content	Purpose
Interval of research	Patient survey should be done at 5 years intervals. Research (beds and department) for medical institutions may be done between 5 years intervals, if it is necessary.	The change of ASEI can be determined at 5 years interval.
Count of diseases	Not only one disease but also multiple diseases should be counted for one patient	The research will be done realistically in old age groups.
	Diseases were recorded in research day	Prevalence should be estimated
Patient survey and optional research - 1	In the model area represented by the sample area, patients for ASEI in research day should be retrospectively checked for other diseases within the past 5 years	The number of persons who suffered from the change to another disease (RPCA) should be determined for the calculation of ASEI
Optional research – 2 (estimated cure rate and estimated potential incidence ratio (EPIR) research)	The model area should be prepared for the representation of the sample area, and the patients for the ASEI in the model area should be recorded with the address, age, and incidence time for research of the cure in the next 5 years The patients for the ASEI in the model area should be researched retrospectively whether they have been cured from the diseases within the past 5 years	The preparation for the calculation of the estimated cure rate (ECR) and estimated potential incidence ratio (EPIR). ECR should be calculated
Optional research – 3 (research for EPIR)	The number of patients in the model area with chronic diseases to be calculated for ASEI should be researched within 1 year and the preparation should be done for the research for the periods of diseases in patients who will be cured within the next 5 years The number of potential patients in the model area with chronic diseases to be calculated for ASEI will be calculated or researched within past 5 years and these numbers will be divided by the number of patients within 1 year and EPIR is calculated.	The preparation should be done for the calculation of EPIR Calculation for EPIR

survey is shown in Table 4.

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Secretariat, Ministry Of Health, Labour and Welfare of Japan, for providing the information required.

ABBREVIATIONS

ASEI, Age-specific estimated incidence rate; **DM**, diabetes mellitus; **ECR**, estimated cure rate; **EPIN**, estimated potential incidence number; **EPIR**, estimated potential incidence ratio; **ICD**, international classification of diseases; **RPDA**; rate of persons who suffered from one disease but died from another disease; **RPCA**, rate of persons who suffered from a disease that developed into another disease; **SE**, standard error.

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Full Length Research Paper

Human metapneumovirus infections in adults associated with respiratory illness in Sao Paulo, Brazil

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The human metapneumovirus was associated with respiratory infections among children without others etiologic causes attributable. Researchers worldwide subsequently detected the virus in samples from all age groups. Our study was established on adults presented with acute respiratory infections from 2001 to 2003. Three groups of outpatients were enrolled: community patients, health care workers and kidney transplant recipients. Routine detection for seven different viruses was undertaken and negative results were set up for reverse transcription polymerase chain reaction (RT-PCR) with primers targeted to hMPV's F gene. Twenty four out of 185 patients (12.97%) were considered positive after amplification of a 347 bp fragment. The virus was detected from June to September in the 2001 to 2002 periods, peaks were higher than 2003 and circulation began earlier in that year. Patients older than 51 years were associated with the infection ($p = 0.006$). Community cases exhibited a higher incidence (18.92%, 11/59) than that of health care workers (10.75%, 10/92) and transplant patients (8.82%, 3/34). No characteristic symptoms could be associated with hMPV infection. Transplanted patients were less symptomatic than the other groups evaluated. Metapneumovirus infections should also be considered within the diagnostics possibilities of respiratory viruses in adult population.

Key words: Human metapneumovirus, epidemiology, reverse transcription polymerase chain reaction (RT-PCR).

INTRODUCTION

The human metapneumovirus (hMPV) was first described in 2001 by van den Hoogen (van den Hoogen and de Jong, 2001) as a paramyxovirus associated with a range of clinical syndromes including colds, bronchiolitis, exacerbations of asthma and obstructive airways disease, pneumonia, and occasionally severe infections in immunocompromised hosts. This virus has been associated with acute respiratory tract infections in young children worldwide (Jartti and van den Hoogen, 2002; Peret and Boivin, 2002; Williams and Martino, 2005; Kahn, 2006) and also in adults as well (Falsey, 2008; Johnstone and Majumdar, 2008).

Respiratory infections are responsible for mild illness in immunocompetent children and adults but morbidity and

mortality are higher in the very young and very old as well; most of the available data on the clinical manifestations of hMPV infection are from studies of children where the virus causes upper respiratory tract infections, bronchiolitis and pneumonia. Recipients of solid organ transplants also are at increased risk (Ison and Hayden, 2002; Kahn, 2006; van den Hoogen, 2007). Health Care Workers (HCW) which are exposed to respiratory infections daily has been shown by our previous study to be at greater risk to acquire viral infections (Bellei and Carraro, 2007a). Several studies have described the hMPV infections in children as common place within this age group but more studies are needed to better characterize these infections in Brazilian adults (Hamelin

Table 1. Characteristics of 185 patients selected for hMPV investigation at Hospital Sao Paulo.

Characteristics	Patients (%)	Mean	Median
Sex			
Male	63(34.05)		
Female	122(65.94)		
Age			
Time of symptoms onset		37.34	36
Exposure to children(≤5yrs)	61(34.07)	4.93	3.5
Origin			
Health Care Workers	92(49.72)		
Community	59(31.89)		
Kidney transplanted	34(18.37)		

and Boivin, 2005; Sumino and Agapov, 2005; Williams and Martino, 2005).

Therefore our report aims to describe clinical and laboratory data of infections caused by this virus from three distinct adult populations from 2001 to 2003 from Sao Paulo.

MATERIALS AND METHODS

The study period began in June 2001 and was concluded in September 2003. Subjects enrolled were adults referred by the attending physician at the emergency room, HCW and kidney transplant patients were enrolled from the outpatient office of the Nephrology Division at Sao Paulo Federal University.

Inclusion criteria

Adults (≥ 18 years) were considered eligible after evaluation by a physician, if presented with any acute respiratory infection (ARI) of possible viral etiology. Influenza-like illness (ILI) was defined when the patient reported fever with at least one respiratory symptom (cough, sore throat or nasal congestion) plus one constitutional symptom (headache, myalgia or chills).

Sample collection

Each patient was interviewed and had one nasal wash sample collected by our researcher. The samples were sent on ice to the Virology Laboratory for immediate storage. Direct fluorescence assay (DFA) was performed immediately and duplicate aliquots of each sample were frozen in -80°C for further analysis by PCR and for virus isolation.

Respiratory virus assays

After centrifugation, the cell pellet was fixed in two slides for the DFA, which screens for Influenza A and B, parainfluenza 1, 2 and 3, adenovirus and respiratory syncytial virus in a two-step procedure, according to the manufacturer's instructions (Light Diagnostics Simulfluor® Screen and Panel, Chemicon Int., Canada). Negative samples were tested by RT-PCR for Picornavirus and

Coronavirus OC43 and 229E according to the methods described previously. The 185 negative samples from 412 patients evaluated through those tests described were further analysed by another RT-PCR assay to detect hMPV viral gene. Negative samples were chosen for this study to evaluate the impact of this virus alone in the populations accessed and also to evaluate the clinical symptoms that could be associated with the infection, disregarding co-infections as a potential confounding parameter.

Reverse transcription polymerase chain reaction (RT-PCR)

Total viral RNA was extracted using QIAamp Viral RNA extraction kit (Qiagen, USA), according to the manufacturer's instructions. The hMPV's 347nt nucleoprotein fragment used flanking primers was designed by Falsey (2008) and the reaction was conducted as described below. Eight microliters of extracted RNA were added to a mix containing 100 U of M-MLV (Invitrogen, USA), 4 µl of 5× first strand buffer, 2 µl of DTT, 1 µl of dNTP mix (2 mM each), 2 µl of primer FR (25 µM) plus 15 U of RNAGuard (Amersham, USA) and molecular biology grade water to a final volume of 20 µl. The mixture was maintained on ice until the enzyme was added, then it was submitted to one hour at 37°C followed by an inactivation step of 70°C for 15 min in a PCT200 MJ Research thermocycler.

Two and a half microliters aliquots of each cDNA sample produced in the first step were used in the PCR. A mixture containing 2.5 µl of 10× buffer solution, 2.5 µl molecular grade glycerol 50% (v/v) (Invitrogen, USA), 2 µl of MgCl₂ (25 mM), 2 µl of a 25 µM primer FF, 0.5 µl of a dNTP mix (20 mM each) plus 2.5 U of Taq polymerase (Promega) was added to each reaction tube containing molecular biology grade water to a final volume of 25 µl. The reaction was conducted at 95°C for 5 min followed by 40 cycles of 94°C for 30 s, 53.2°C for 30 s and 68°C for one min. A final extension step of 10 min at 72°C and then maintained at 4°C until a electrophoresis on a 2% agarose gel was performed.

Statistical analysis

To correlate positive with negative cases distributions between the groups a χ^2 (chi-square) partition test for numerical data alongside with Fishers exact test and Students T test, epidemiological and clinical variables were analyzed. Level of significance was established at less than 0.05 ($\alpha \leq 5\%$). Calculations were done with Microsoft Excel version 2010-SP1.

RESULTS

From June 2001 to September 2003, one hundred and eighty five patients previously tested negative for other viruses were enrolled for the study. Subjects mean age was 37.3 years (median of 35 years), 66% of those patients were female and 34% had contact with children under five years old. Risk group distribution and symptoms duration are shown in Table 1.

The RT-PCR for hMPV was positive in 24 (12.97%) patient's nasal washes. Figure 1 represents hMPV infections in a monthly distribution during the study period. All hMPV positive samples were identified within winter months and no gaps were found during its season, but the variations that were found were in accordance with the risk groups studied. The age distribution of hMPV infections had a high probability of association ($p = 0.006$) when the group of patients with the elderly (51+

Table 2. Distribution of positive and negative cases according different risk group of patients during the study period.

Year	2001		2002		2003	
	Positive	Negative	Positive	Negative	Positive	Negative
Population						
Community	1	20	0	13	10	15
Health care workers	1	15	2	51	7	16
Kidney transplanted	0	0	2	20	1	11
Total	2	35	4	84	18	42

Table 3. Clinical symptoms frequencies among hMPV positive and negative cases different risk group of patients investigated during the study period.

Symptom	Health care workers (%)		Community (%)		Renal transplant (%)	
	Positive (n=10)	Negative (n=83)	Positive (n=11)	Negative (n=47)	Positive (n=3)	Negative (n=31)
Fever	40	64	81	74	0	29
Cough	70	78	91	79	67	77
Coryza	90	84	91	72	67	81
Sore Throat	50	67	73	68	33	39
Headache	90	73	73	70	33	55
Myalgia	90	78	55	66	67	48
Chills	50	53	55	49	0	26

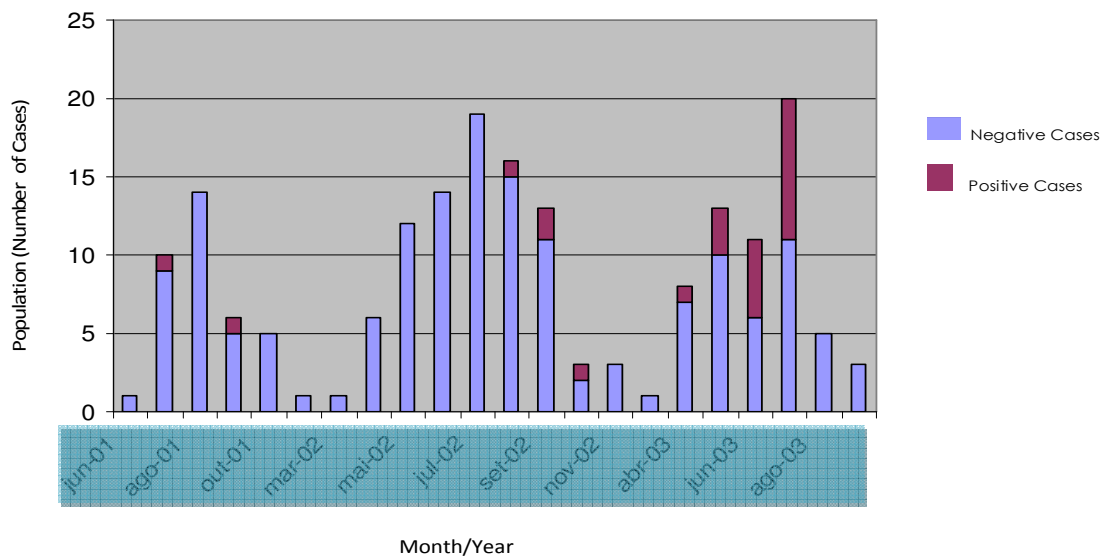


Figure 1. Laboratory confirmed hMPV infection cases distribution among adult population presenting with acute respiratory infection from 2001 to 2003.

y.o.) was compared to the group with younger patients from all groups.

The variable “contact with patient” was not associated with higher risk of hMPV infection for the HCW population, clinical data shown in Table 1. The history of household or professional contact with a child with less than 5 years old was also not associated with higher risk for infection. Cases from the community had higher positivity results (18.92%, 11/59; symptoms associated with this group are shown in Table 2), particularly in 2003. Health care workers and kidney transplant patients had 10.9%

(10/92) and 18.6% (11/34) positivity, respectively.

All positive samples were collected from patients that had symptoms in 5.1 days on average (mean 4.9 days). ILI case definition was reported by 45.8% of positive cases except for transplant patients, this group did not present with ILI at that moment. In all, the transplant positive cases were less symptomatic than the other groups evaluated together. The clinical data revealed that hMPV positive cases presented mainly coryza (87.5%), cough (79.1%) and headaches (75%) but this data was not statistically significantly different from negative cases

(Tables 1 to 3).

DISCUSSION

The hMPV incidence among the adult population from different risk groups from Sao Paulo, Brazil was accessed by this work. Negative cases from previously immunofluorescence screened cases, from three distinct groups of patients (community population, health care workers and kidney transplant) over three years, were analyzed by RT-PCR reactions and their clinical data correlated with the results. All hMPV positive samples were identified within winter months. This winter pattern concur with previous studies regarding the circulation period for this virus (Falsey and Erdman, 2003; Falsey and Criddle, 2006).

Our study detected this virus in 12.97% of the negative samples tested. This reflects that hMPV is present in approximately one in each ten adults presented with respiratory symptoms in our population, without any other confirmed viral infection. Considering that there are few case reports available for hMPV infections in adults and/or in the elderly from Brazil, limited conclusions can be drawn and more epidemiological studies are needed to confirm the data. In Brazil, Cuevas et al. (2003) investigated 120 children for hMPV infections and found 15.2% of positive cases among them, a incidence that is much higher than the one found by our study, since this group is at more risk of infection and at greater risk of coming into contact with other children, higher positivity rates were expected; but in comparison to our study groups, the assays exhibited an overall comparable result, a more detailed and prospective study must be conducted to identify variables attributable to this infection within these groups in order to better understand some of the symptoms observed in the patients studied here.

Previous studies found that positive cases of hMPV infections in adults presenting with ARI had incidences ranging from 2.2% (Stockton and Stephenson, 2002) to 3.4% (Falsey and Erdman, 2003). Kaye et al. (2006) found 5.4% of hMPV infections in adults from the community, a result that is similar to the incidences observed in 2001 and 2002 of our study. In 2003, there was a raise in positivity up to 30%, which in turn could be explained by different subtype prevalence as observed and hypothesized by Gerna et al. (2005), whose similar results were further confirmed to be due to different subtype circulation. Since our study was primarily concerned with establishing ARI etiology within the three samples studied, no such claim can be made to whether viral subtype is responsible for the differences in cases observed here.

The association between advanced age and infections by hMPV suggested by other authors (Boivin and Abed, 2002; Falsey and Erdman, 2003; Honda and Iwahashi, 2006) was also found by our study when comparing the all samples together ($p = 0.006$). Patients older than 51

years had more infections by hMPV than the other four age groups. Such an association was also described by Kaye et al. (2006). The twenty positive samples for hMPV, out of the 373 obtained, had 50% of those positive cases belonging to that age group (< 75 y.o.) in that report.

No previous detection of hMPV in kidney transplanted patients was reported here in Brazil. Our results for this population showed fewer positive cases than those published by Larcher et al. (2005) whose group identified the virus in 25% of lung transplant recipients. It is also important to notice that we recruited patients from our ambulatory and most hMPV studies to date were based on hospitalized patients, which might overestimate its incidence. The transplanted patients evaluated here were less symptomatic than the other two groups. The positive cases had even less symptoms, with an exception made for myalgia; without statistical significance (67 versus 48%; $p > 0.05$). These findings may reflect that the treatment protocols that the transplant recipients undertake, such as corticosteroids plus immunosuppressive therapy, may be a reason for masking flu-like symptoms (Bellei and Carraro, 2007b; Vu and Bridevaux, 2011).

All three population's clinical aspects did not reveal typical symptoms for predicting hMPV infections (Tables 1 to 3). Falsey et al. (2003) previously reported no evidence for an association between fever and hMPV infections, however, the same group in another report (Falsey and Criddle, 2006) show that 80% of hMPV cases studied had fever, against 48% from control cases. This suggests that this factor may still be under unidentified conditions.

Our results point to a significant percentage of hMPV infections in adults from Hospital Sao Paulo. Community acquired hMPV infections affects nearly one out of five patients without a diagnosed etiology presented with influenza-like illness during winter months according to our results. Our study was not designed to detect hMPV co-infections and from this reason, the clinical data described here were directly associated with hMPV. This study suggests that hMPV is a frequent pathogen among adults in Brazil. Metapneumovirus infections should also be considered among the most common respiratory viruses by the attending physician in periods of respiratory viruses with known circulation.

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Full Length Research Paper

Perception, attitude and involvement of men in maternal health care in a Nigerian community

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This study aimed to examine men's perception, attitude and involvement in maternal care. A cross-sectional descriptive survey was carried out in Atelewo community in Osogbo, Osun State, Nigeria using multi-stage sampling technique to select 400 respondents. Participants were adult men of reproductive age. Data were collected using semi-structured questionnaire. In the study, there was no intervention component; and main outcome measures were perception of men about maternal health, attitude of men to maternal health and involvement of men in maternal care. Results revealed majority of the respondents 225 (62.2%) were within the age group 20 to 39 years with a mean age of 36.3 years \pm 10.86. Most of them were skilled workers 144 (39.8%) and many 147 (40.6%) had post primary school education. One hundred and eighty-six (51.5%) of the respondents had poor knowledge while 205 (56.5%) had a good attitude towards maternal health care. Concerning the involvement of the men in maternal health care of their wives, about a quarter 62 (29.1%), 87 (24.0%), 98 (27.1%) ever followed their wives to family planning clinic, ante-natal clinic and the delivery room respectively. Thus, the level of awareness of men about maternal health was high, but their involvement in giving care was poor and only about half of them had good attitude towards maternal health care. Education and awareness programs should therefore be carried out by governmental agencies, non-governmental organizations and other voluntary groups to address involvement of men in maternal health care.

Key words: Perception, attitude, involvement, maternal health, reproductive health, men, women.

INTRODUCTION

Maternal health refers to the broad apparent and currently accepted means of providing promotive, preventive, curative and rehabilitative health care for mothers (Lucas and Gilles, 2003). It refers to health of women during pregnancy, childbirth and postpartum period and it is a very important component of reproductive health. Maternal health in developing countries and economically restrained settings remains a

daunting and largely unmet global public health challenge (Taiwo et al., 2007). Progress has been slow and some countries with high maternal mortality are experiencing stagnation or even reversals (WHO, 2000; WHO, 2006) with countries in sub-Saharan Africa, including Nigeria being the hardest hit (UNICEF, 2006; NPC, 2004). Nigeria has one of the worst maternal health indicators in the world (Joseph et al., 2009; Federal Ministry of Health

2003; Jose, 2010), however current progress in maternal mortality ratio reveals 32% reduction from 800 to 545 deaths per 100,000 live births (Jose, 2010). Over the years, the issue of maternal health has been predominantly seen and treated as a purely feminine matter. The hugely disproportionate representation of men, and their resulting dominance, among those responsible for the planning and provision of health care, has had serious consequences for the health status of women and girls, particularly in developing countries (Taiwo et al., 2007). Before the current concern for male involvement began, reproductive health issues and services had become synonymous with women's reproductive health, and men were assumed to have no special role in such matters. However, the exclusion of men from active involvement in these issues represents a lack of appreciation of the social reality of daily living in most developing societies, particularly in Africa. Indeed, the characteristic lack of male involvement in reproductive initiatives, including family planning, is a major obstacle to a speedy fertility decline in sub-Saharan Africa given the considerable authority and power vested on men as decision makers in the home and society (Drennon, 1998).

In most African countries, maternal health issues which include family planning, pregnancy and childbirth have long been regarded exclusively women's affairs (Mullick et al., 2005). Although the health of mothers are determined by many factors including socio-economic status and environmental factors, one important and crucial factor that has been neglected over the years is the role of men as a determinant of health of mothers (Mullick et al., 2005).

Men's involvement in reproductive health is crucial, though their participation has been poorly demonstrated. Factors responsible for this include culture, religion, ignorance and socio-economic factors. Men are the primary decision makers of most families in developing countries, as such their involvement in maternal health issues could promote a better relationship between couples in the family and enhance maternal wellbeing (Mullick et al., 2005). It has been observed that men's involvement in maternal health is a promising strategy for promoting maternal health (Cohen et al., 2000; Mullay et al., 2005) observed that involving husband/partner and encouraging joint decision-making among couples may provide an important strategy in achieving women's empowerment; this will ultimately result in reduced maternal morbidity and mortality. It has also been observed that men's behavior and involvement in the maternity care of their pregnant partners can significantly affect the health outcomes of the women and babies (Stycos, 1996). Men could be involved in maternal health care in the following ways: supporting contraceptive use by women, helping pregnant women to stay healthy, arranging for skilled care during delivery, avoiding delays in seeking medical care, helping after the baby is born, and being responsible fathers (effective parents) (Joseph et al.,

2009).

In Nigeria, where culture has been shown to be an important factor influencing relation to women's access to available reproductive health facilities, there is paucity of data on men's views with regard to maternal health (Yahaya, 2002; Wall, 1998). This study, therefore, aimed to assess the perception, attitude and involvement of men in maternal health care. This will help in understanding men's disposition and serve as a guide in designing targeted programs.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted amongst men. The study location is the Atelewo community in Osogbo, the capital of Osun State, located in the southwestern part of Nigeria and is dominated by the Yoruba speaking ethnic group. The study population included adult males from the age of 18 years upwards residing within the Atelewo community. A systematic random sampling technique was used to select households, and every male aged 18 years and above in the selected households who gave verbal consent was included in the study.

Four hundred pre-tested, semi-structured questionnaires were either self administered when the respondents could read or administered by interviewers when respondents were not able to read. Section A of the questionnaire covers socio-demographic status of respondents (that is, age, educational level, occupation, religion, tribe); Section B covers respondents knowledge on maternal health care [awareness and meaning of various maternal health care services such as antenatal care (ANC), family planning (FP) and post natal services (PNC)]; Section C includes attitude to maternal health care services (Agreeing, indifferent or disagreeing on issues related to men supporting their wife on maternal health care services); Section D covers involvement of respondents in maternal health care services (previous involvement in various maternal health services such as ANC, FP and PNCs).

Proctors who guide the questionnaire administration were trained medical students. Pre-testing and question validation was performed in Offatedo Community, Egbedore Local Government Area of Osun State.

Measurement of outcome measures

The questions on attitude and involvement of the respondents about maternal health services were scored. Attitude and individual involvement was calculated. Those with wrong responses are scored 0 while those with right responses are scored 1. Respondents who score below the mean were regarded as having poor knowledge, negative attitude or poor involvement in maternal health services as the case may be while those with scores up to or above the mean were regarded as having good knowledge, attitude or involvement.

Data analysis

The data were analyzed using Statistical Package for Social Sciences (SPSS) version 16. Chi-square was used to test for statistical significant associations between categorical variables and the level of significance was set at 0.05.

Ethical considerations

Ethical clearance was obtained from the Ethical Committee,

Table 1. Socio-demographic characteristics of respondents (n=362).

Socio-demographic characteristics	Frequency	Percentage
Age group (years)		
<20	7	1.9
20-39	225	62.2
40-59	114	31.5
60 and above	16	4.4
Marital status		
Single	69	19.1
Married	281	77.6
Divorced	5	1.4
Widowed	7	1.9
Occupation		
Unemployed	40	11.2
Unskilled	114	31.7
Skilled	144	39.8
Professionals	63	17.43
Educational status		
No formal education	11	3.0
Primary education	60	16.6
Secondary education	144	39.8
Tertiary education	147	40.6
Religion		
Christianity	174	48
Islam	186	51.4
Others	2	0.6
Ethnicity		
Yoruba	354	97.8
Igbo	8	2.2
Hausa	0	0.0

LAUTECH Teaching Hospital, Osogbo, and verbal informed consent was sought from each respondent. Only those who consented were included in the study.

RESULTS

Socio-dermographic status of respondents

Majority of the respondents 225 (62.2%) were within the age group 20 to 39 years with a mean age of 36.3 ± 10.86 years. Most of them were married 281 (77.6%), skilled 144 (39.8%), had post secondary education 147 (40.6%), Muslims 186 (51.4%) and of the Yoruba tribe 354

(97.8%) (Table 1).

Perception about maternal health care (MHC) among respondents

Most of the respondents 358 (98.9%) were aware of the need for maternal health care. Majority 345 (95.3%) had heard of family planning before, and many of those that were aware understood it to mean control of family size 130 (37.7%) and child spacing 120 (34.8%). Of the 345 who had heard about family planning before, 309 (89.5%) knew that men had a role in family planning and 281

Table 2. Awareness and knowledge of respondents on maternal health care (MHC).

Variable	Frequency	Percentage
Aware women need special care (n=362)		
Yes	358	98.9
No	4	1.1
Ever heard of family planning (n=362)		
Yes	345	95.3
No	17	4.7
Meaning of family planning(n=345)		
Control of family size	130	37.7
Child spacing	120	34.8
Prevent unwanted pregnancy	95	27.5
Men's role in family planning(n=345)		
Consent	64	18.6
Support	281	81.4
Contraceptive methods for men (multiple response; n=362)		
Vasectomy	70	19.3
Male condom	338	93.4
Injectables	226	67.9
Diaphragm	46	13.8
Ever heard of ANC (n=362)		
Yes	340	93.9
No	22	6.1
What ANC entails (n=340)		
Taking care of pregnant women and their fetuses	268	78.8
Giving drugs and injection to pregnant women	41	12.1
Detecting and managing complication	31	9.1
Men's role in ANC (n=340)		
Financial support	99	29.1
Encouraging and reminding her	104	30.6
Providing emotional and moral support	137	40.3
Men should ensure skilled hands for delivery (n=362)		
Yes	355	98.1
No	7	1.9
Reasons for ensuring skilled hands for delivery (n=355)		
Good health of mother	23	6.5
Proper care of mother	48	13.5
Safe delivery	145	40.8

Table 2. Cont'd.

Avoid complications	139	39.2
Know wife needs care and support after delivery(n=362)		
Yes	360	99.4
No	2	0.6
Awareness of exclusive breastfeeding(EBF) (n=362)		
Yes	261	72.0
No	101	28.0
Understanding of EBF(n=362)		
Breast milk alone	265	73.2
Breast milk with little water	97	26.8
Duration of EBF(n=362)		
<6	79	21.8
6	199	55.0
>6	84	23.2

(81.4%) understood the role to be supportive. Respondents were asked an open ended question about male specific contraceptive methods, majority, 338 (93.4%) knew male condoms followed by injectables 226 (67.9%), 70 (19.3%) knew vasectomy with the diaphragm being the least known 46 (13.8%) contraceptive. In addition, most of the respondents 340 (93.9%) had heard of ANC. Some of those who had heard about ANC believed it entails taking care of pregnant women and their unborn child 268 (78.8%) while others believed it involves giving drugs and injections to pregnant women 41 (12.1%) and managing/detecting complications 31 (9.1%). Many 137 (40.3%) saw their role as providing emotional and moral support while some 99 (29.1%) felt financial support is their only role. Also majority of the respondents 348 (96.1%) believed that men had a role to play in deciding where their wives delivered and 355 (98.1%) knew they should ensure their wives were delivered by skilled birth attendants. The main reasons given for ensuring skilled hands at delivery were to ensure safe delivery 145 (40.8%) and to avoid complications 139 (39.2%). Also, 360 (99.4%) knew their wives needed care and support from them after delivery. An appreciable number of respondents 265 (73.2%) understood what exclusive breastfeeding (EBF) meant and 199 (55.0%) were knowledgeable about the correct duration of six months. After the scoring of outcome variables, 186 (51.4%) and 176 (48.6%) of the respondents had poor and good comprehensive knowledge about maternal health care (MCH) respectively (Table 2).

Attitude of respondents to maternal health care (n=362)

Table 6 shows the attitude of respondents towards maternal health care. Most of the respondents 333 (93.1%) agreed that men should encourage pre-conception care, encourage family planning 308 (85.1%) and that men should support exclusive breast feeding 338 (93.4%). However, 156 (43.1%) still felt that family planning encourages promiscuity. The outcome variables for attitude were scored, and 157 (43.4%) were found to have negative attitudes, while 205 (56.6%) had positive attitudes towards maternal health care (MCH) (Table 3).

Involvement of respondents in maternal health care

The wives of 193 (53.2%) respondents had used family planning (FP) methods before, but only few 105 (29.0%), 87 (24.0%), 98 (27.1%) had ever followed their wives to family planning clinics, antenatal care and to the labour room respectively. The categorized involvement of men in maternal health care after scoring of the outcome variables showed that 194 (53.6%) had poor involvement, while 168 (46.4%) had good involvement (Table 4).

Association between socio-demographic characteristics of respondents towards perception, attitude and male involvement in maternal health

The categorized knowledge about MHC was found to be

Table 3. Attitude of respondents to maternal health care (n=362).

Variable	Frequency (Percentage)		
	Agree	Indifferent	Disagree
Men should encourage pre conception care	333(93.1)	8(2.2)	17(4.7)
Men should encourage FP	308(85.1)	7(1.9)	47(13.0)
FP encourages promiscuity	156(43.1)	71(19.6)	135(37.3)
FP could lead to infertility	118(32.6)	108(29.8)	136(37.6)
Men should follow their wives for ANC	231(63.8)	39(10.8)	92(25.4)
ANC encourages gossip	71(19.6)	57(15.7)	233(64.4)
ANC encourages promiscuity	65(18.0)	42(11.6)	255(70.4)
Men should provide finances for ANC	330(91.2)	6(1.7)	26(7.2)
Men should decide place of delivery	347(95.9)	15(4.1)	0(0.0)
Men should be present in labour room	147(40.6)	52(14.4)	163(45.0)
Men should assist with house chores	288(79.6)	25(6.9)	49(13.5)
Men should ensure child complete immunization	353(97.5)	6(1.7)	3(0.8)
Men should support EBF	338(93.4)	12(3.3)	12(3.3)
Breast milk alone is not sufficient for children <6 months	170(47.0)	21(5.8)	171(47.2)
Herbal concoction is needed to prevent childhood illness	131(36.2)	19(5.2)	210(58.0)

Table 4. Involvement of respondents in maternal health care.

Variable	Frequency (percentage)	
	Yes	No
Wife ever used family planning (n=362)	193(53.2)	169(46.8)
Informed by wife before use of FP (n=362)	249(68.8)	113(31.2)
Gave consent before wife used FP (n=362)	234(64.6)	128(35.4)
Followed wife to FP clinic (n=362)	105(29.0)	257(71.0)
Wife currently on FP (n=362)	157(43.4)	205(56.6)
Allow wife to attend ANC (n=362)	353(97.6)	9(2.4)
Ever followed wife to ANC (n=362)	87(24.0)	275(76.0)
Ever followed wife to labour room (n=362)	98(27.1)	264(72.9)
Aware of the immunization status of your child(ren) (n=362)	302(84.3)	60(16.6)
Children were exclusively breast fed for 6 months (n=362)	263(72.6)	99(27.4)
Will follow wife to delivery room next pregnancy (n=362)	190(52.4)	172(47.6)

significantly associated with the respondents' marital status ($p = 0.039$), with the ever married having a better knowledge than the single. The involvement of men in maternal health care was also found to be significantly associated with the respondents' age ($p = 0.0001$), marital status ($p = 0.0001$) and occupation ($p = 0.009$), such that those older than 40 years, ever married and professionals were more involved in maternal health care (MCH). The categorized attitude was found to be significantly associated with the occupation ($p = 0.015$) and educational status (0.001) of the respondents, with professionals and those with tertiary education having more positive attitude (Table 5).

DISCUSSION

The study demonstrates key issues in respect of

perception, knowledge, attitude and involvement of men in maternal health care in a Nigerian community. The demographic pattern shows that majority of the respondents (62.2%) were found within the age groups of 20 to 39 years; this meant that most men in Atelewo community were still within their active reproductive years. In most Nigerian communities, the population structure reflects a preponderance of young persons with only a small proportion of the elderly and aged, indicative of a population with high fertility (National Population Commission, Federal Republic of Nigeria, Nigeria Demographic and Health Survey, 2003). The educational status of men in the community can be considered to be more than average since most (about 80%) of them had at least secondary school education. In contrast, in Nigeria, only 72.5% of men were found to be literate. Globally, more than half a million women still die annually

Table 5. Association between attitude towards male involvement in maternal health care and socio-demographic characteristics of respondents (n=362).

Variable	Attitude (%)		X ²	p-value
	Poor	Good		
Age group				
<40	99(64.7)	127(63.8)	0.030	0.863
40 and above	54(35.3)	72(36.2)		Not significant
Marital status				
Single	27(17.6)	38(19.1)	0.121	0.728
Ever married	126(82.4)	161(80.9)		Not significant
Occupation				
Skilled	58(38.4)	81(41.3)	10.466	0.015
Unskilled	61(40.4)	50(25.5)		Significant
Unemployed	12(7.9)	24(12.2)		-
Professionals	20(13.2)	41(20.9)		-
Educational status				
No formal education	9(5.9)	2(1)	15.569	0.001
Primary education	26(17)	33(16.6)		Significant
Secondary education	70(45.8)	68(34.2)		-
Tertiary education	48(31.4)	96(48.2)		-
Religion				
Christianity	72(47.1)	102(51.3)	1.825	0.402
Islam	80(52.3)	97(48.7)		Not significant
Others	1(0.7)	0(0.000)		-
Income grouping				
<18,000	32(30.5)	44(29.5)	0.026	0.871
18,000 and above	73(69.5)	105(70.5)		Not significant

as a result of complications of pregnancy and childbirth (WHO, 2005). A disproportionately high burden of these deaths is borne by developing countries, including Nigeria. With maternal mortality ratio of 1,500 per 100,000 births and an estimated 55,000 deaths annually, Nigeria accounts for nearly 10% of the global estimates of maternal mortality (Adetoro, 1987). In order to address this disturbing trend, the International Conference on Population and Development (ICPD) urged that special efforts be made to emphasize men's shared responsibility and promote their active involvement in maternity care (UNFPA, 1995). Almost all the respondents (98.9%) from this study were aware of the need for maternal health care and 4 out of 10 believed that provision of basic needs is an important role of men in maternal health care. This corroborates other studies on men's role of caring in maternal health (Stycos, 1996; Berer, 1996; Helzner (1996). Similar studies on the participation of men in maternal care have been reported mostly from

southern part of Nigeria (Odimegwu et al., 2005). Odimegwu et al. (2005) reported a high level of awareness and participation of men in maternity care in Osun State.

The promotion of family planning, so that women can avoid unwanted pregnancy, is central to the World Health Organization (WHO) work on improving maternal health and is core to achieving the Millennium Development Goal (Morhason-Bello et al., 2008). Family planning being one of the essential interventions in improving maternal health is known by majority of the respondents and nearly all of them accepted that men have roles to play in family planning. These findings are similar to previous studies on male participation in reproductive health in Ghana (Berer, 1996; Helzner, 1996; Male Participation in Reproductive Health, 1998).

Also half of the respondents agreed that men should be involved in pre-conception care and also encourage family planning; this corroborates other previous studies

that has been carried out in South Africa (Mullick et al., 2005; Population Reports, 1998).

Findings on family planning involvement might be attributed to increase awareness of family planning services and methods as a way of promoting maternal and child health and the gradual and progressive acceptance of it by men generally.

Men being critical partners for the improvement of maternal health and reduction of maternal mortality can be clearly demonstrated in the area of antenatal care (ANC) of which their social, emotional and economical inputs cannot be underestimated. ANC awareness of the respondents were very encouraging, nearly all of them demonstrated a high level of awareness. About attitude towards antenatal care, nearly half of the respondents agreed that men should accompany their wives for antenatal care visit, with a similar finding about the role of partners during maternity in a study on involving men in maternity care (Andrews, 2012). However only 2 out of 10 respondents follow their wives for antenatal care visits and also to the labour ward, findings which are in keeping with other studies (Mullick et al., 2005; Britta, 2005).

Men's presence and their participation at the health facilities during antenatal care visit of their wives will help boost the morale of their wives and also bring about a greater sense of commitment of both parents to having healthy mothers and babies as evident from other studies (Mullick et al., 2005; Cohen et al., 2000; Mullay et al., 2005; Stycos, 1996).

Perception of ANC amongst respondents showed that about four-fifth believed it entails taking care of pregnant women and their unborn child while few believed it involves giving drugs and injections to pregnant women and detecting complications. However less than half of the respondents saw their role as providing emotional and moral support while 2 out of 10 felt financial support is their only role, these findings are not in keeping with the general expectations of men described in other studies (Joseph et al., 2009; Mullick et al., 2005; Cohen et al., 2000; Mullay et al., 2005). This therefore stresses the need to target men for enlightenment programs about maternal health care, and to involve men in the design and implementation of maternal health services.

Postnatal care is one of the most important maternal health-care services for not only prevention of impairment and disabilities but also reduction of maternal mortality. In line with perception to delivery and post-natal care, nearly all the respondents believed they had a role to play in deciding where their wives deliver, ensuring that their wives were in skilled hands for delivery and also in the aspect of them giving the necessary care and support after delivery and during peuperium. These findings were similar to the outcome of the research on men in South Africa and maternity care (Ezeh et al., 1996). This pattern is encouraging and further underscores the need for men to be more involved in the design and implementation of maternal health services.

Professionals and those with tertiary education were also found to have better attitude towards MHC than the others. This pattern has been similarly reported by earlier studies and it may not be difficult to understand. The knowledge and involvement in MHC was found to be associated with marital status with the ever married having better knowledge and involvement in MHC than the singles, and this also is easy to understand. It however raises the need to begin educational programs about MHC early, even before the men get married.

Maternal deaths are still high in developing countries most especially in Nigeria, the cause of which is multi-factorial. Maternal health care has been seen to be more of a feminine affair with women being at the receiving end of unfavorable pregnancy and delivery outcomes. Men's role in maternal health care is cardinal and of great importance in the attainment of MDGs 4 and 5; reducing child mortality and improving maternal health, respectively.

CONCLUSION AND RECOMMENDATION

The knowledge and attitude of respondents towards maternal health care were average, and their involvement in the health care of their wives was low as almost a quarter of respondents had ever followed their wives to family planning clinics, antenatal clinics and delivery rooms. This still shows that men lag behind in their responsibilities in improving maternal health.

Enlightenment programs should therefore be carried out by governmental agencies, non-governmental organizations and other voluntary groups and religious bodies to stress the involvement of men in promoting maternal health care and also being agent of change in improving the quality of life of women as it relates to maternal health thereby bringing about healthy families and indeed healthy nation.

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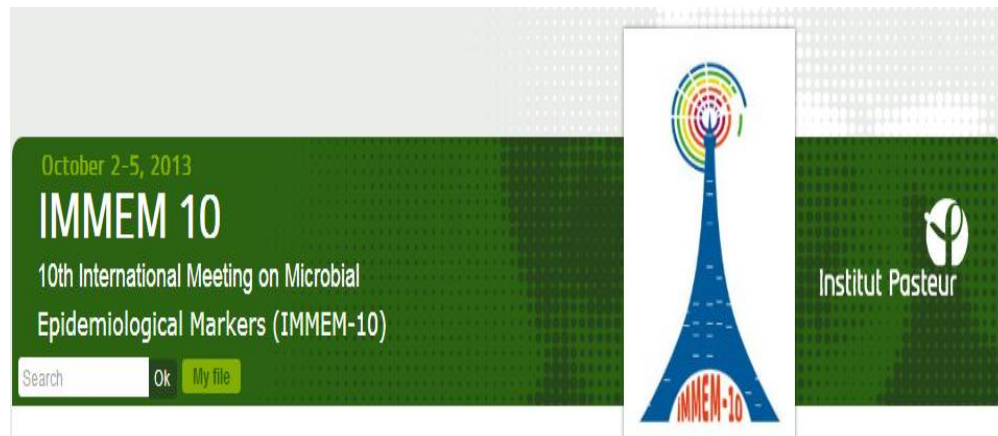
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